Remarks

Upon entry of the foregoing amendment, claims 157, 159-160, 162-163, 165-166, 168-176, 179-180, 182-183, 185-186, 188-189 and 191-287 will be pending in the application. Claims 158, 161, 164, 167, 177, 178, 181, 184, 187, 190 and 288-294 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the unamended claims in a continuing application.

Claims 157, 159, 162, 165, 168, 173, 176, 180, 182, 185, 188, 191, 196, 199, 207, 210, 230, 231, 232, 236, 239, 247, 250, 257, 260, 264, 273 and 276 have been amended as discussed during the recent Examiner interview. Support for claims 157 and 180 (and dependent claims) as amended can be found in original claims 1 and 11, part (a). As the Examiner requested, Applicants have inserted a paragraph containing the subject matter of original claims 1 and 11, part (a), into the specification at page 6, after line 18.

Claims 159, 162, 165, 168, 182, 185, 188 and 191 were amended to place the claims into proper dependent format. The remaining claims were amended as the Examiner suggested during the Examiner interview.

This amendment introduces no new matter and entry thereof is respectfully requested. Applicants reserve the right to pursue the subject matter of the unamended claims in a continuing application.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Examiner Interview

Applicants thank Examiner Priebe for the courteous and helpful telephonic interview extended to Applicants' undersigned representative on June 24, 2002.

Specification

The Examiner objected to the specification as allegedly failing to provide proper antecedent basis for the claimed subject matter. (Paper No. 34, at page 2.) According to the Examiner, "[t]here is no antecedent basis in the specification as originally filed for claims 159, 162, 165, 168, 182, 185, 188, 191, 229, and 231" and "new claims broadly reciting 'at least 90% identity' in the absence of a recited 'essential property' are not supported in the original disclosure, and accordingly are rejected under 35 USC 112, first paragraph for the introduction of new matter." *Id.* at pages 2-3.

Without admitting to the Examiner's allegation, and solely in the interest of facilitating prosecution, Applicants have amended the claims to recite 95% identity. As the Examiner acknowledged, support for this amendment can be found in original claims 1 and 11, part (a), the subject matter of which was inserted into the specification at page 6, after line 18. Accordingly, this amendment should overcome the objection.

Rejections under 35 U.S.C. § 112

Written description

Claims 157-158, 161, 164, 167, 170-181, 184, 187, 190, 193-202, 207-208, 210-211, 236-237, 239-240, 247-248, 250-251, 257-258, 260-261 and 264-294 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. (Paper No. 34, at page 3.) The Examiner maintained the rejection in the Advisory Action. (Paper No. 37, at page 2.)

Without admitting to the Examiner's allegation, and solely in the interest of facilitating prosecution, Applicants have amended the claims to recite 95% identity. As the Examiner acknowledged, support for this amendment can be found in original claims 1 and 11, part (a), the subject matter of which was inserted into the specification at page 6, after line 18. Accordingly, withdrawal of this rejection is respectfully requested. Applicants reserve the right to pursue the subject matter of the unamended claims in continuing applications.

Regarding claims 176, 196, 199, 207, 210, 236, 239, 247, 250, 260, 273 and 276, the Examiner alleged that "[w]hile the specification fully supports the linkage between heterologous sequences in general to the first nucleic acid, the same cannot be said for an 'operable linkage'." (Paper No. 34, at page 5.) The Examiner maintained the rejection in the Advisory Action. (Paper No. 37, at page 2.)

Without admitting to the Examiner's allegation, and solely in the interest of facilitating prosecution, Applicants have amended the claims to recite that the "polynucleotide comprises a nucleotide sequence heterologous to said first nucleic acid." During the Examiner interview, the Examiner indicated that such an amendment would overcome the rejection. Accordingly, withdrawal of this rejection is respectfully requested. Applicants reserve the right to pursue the subject matter of the unamended claims in continuing applications.

In the Advisory Action, the Examiner indicated that the new matter rejection of claims 177, 197, 200, 208, 211, 237, 240, 248, 251, 261, 274, 277 and 280 was withdrawn. (Paper No. 37, at page 2.)

The Examiner indicated that claims 230, 232 and 264-279 would be allowable.

Applicants have canceled claims 288-294 without prejudice or disclaimer. Thus, the rejection of claims 288-294 has been rendered moot. Applicants reserve the right to pursue the subject matter of the canceled claims in a continuing application.

Enablement

The Examiner maintained the rejection of claims 180-182, 184-185, 187-188, 190-191, 193-202, 229, 231 and 233-242 under 35 U.S.C. § 112, first paragraph. (Paper No. 37, at page 3.) According to the Examiner,

> Applicant mischaracterizes page 16, lines 4-18 of the specification. Lines 4-11 describe using fragments of SEQ ID NO:2 to induce antibodies, lines 12-18 describe other types of sequence variation, and in the context of the following paragraphs, are clearly directed [sic] biologically relevant functions of PDEF, such as in transcription, not making antibodies.

Paper No. 37, at page 3. Applicants respectfully disagree.

Contrary to the Examiner's position, the specification at page 16 explicitly teaches that variants are useful for making antibodies that recognize the PDEF protein. Lines 4-6 teach that although deletion variants may loose one or more biological functions, other biological activities may still be retained. Lines 6-9 teach that one such biological activity is the ability of a deletion variant to induce and/or to bind antibodies which recognize the protein. Lines 9-11 teach that one skilled in the art can easily determine whether a deletion

variant retains such an immunogenic activity using routine methods. Lines 12-13 teach that "[t]hus, the invention further includes PDEF polypeptide variants which show substantial biological activity." Examples of variants mentioned include deletions, insertions, inversions, repeats, and substitutions. Thus, the specification as described *supra*, specifically teaches that the ability to induce and/or to bind antibodies that recognize the PDEF protein is a biological function of PDEF variants, such as deletions, insertions, inversions, repeats, and substitutions.

Moreover, the subsequent paragraphs at pages 16 and 17 provide guidance on how to make phenotypically silent substitutions, as well as conservative substitutions. Thus, in contrast to the Examiner's assertion, the subsequent paragraphs are not "directed to biologically relevant functions of PDEF, such as in transcription." Instead, one area of focus of the description at pages 16 and 17, especially lines 4-18, is on the ability of PDEF variants to induce and/or to bind antibodies that recognize the PDEF protein. Therefore, the specification *does* teach that variants, such as deletions and substitutions, can be used for the purpose of making antibodies against the polypeptide of SEQ ID NO:2.

The Examiner is reminded that the test for enablement is whether the disclosure when filed contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. M.P.E.P. § 2164.01 at 2100-174 (August 2001). The standard applied is whether the experimentation needed to practice the invention is undue or unreasonable. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

Here, Applicants have indicated that the claimed variants are useful for raising antibodies to the polypeptide of SEQ ID NO:2, even if biological activity is not retained.

As stated by the court in *In re Marzocchi*, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971) (emphasis in original). Accordingly, the Examiner has not provided any objective evidence showing that making and using the claimed polynucleotides was not routine to the skilled artisan at the time the invention was filed.

Furthermore, Applicants reiterate that the issue is not whether the specification discloses all possible PDEF polypeptide variants that can be used to make antibodies to the PDEF protein, but rather whether additional PDEF polypeptide variants would be expected to be useful to make antibodies to the PDEF protein, and whether such polypeptide variants can be determined, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. It is thus not necessary to disclose all peptide variants of PDEF that can be used to make antibodies to the PDEF protein, or to limit the claims to the specific polypeptide sequences disclosed in the specification to make antibodies. *See In re Angstadt*, 537 F.2d 498, 502-503, 190, U.S.P.Q. 214, 218 (C.C.P.A. 1976): "To require such a complete disclosure would apparently necessitate a patent with thousands of examples . . . . More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments." *Id.*

Since the disclosed or otherwise known methods of making and screening the claimed polypeptides may be used to determine, without undue experimentation, whether

a given polypeptide encompassed by the claims can be used to make antibodies, the enablement requirement is fully satisfied. *In re Wands*, 858 F.2d at 738, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989).

Furthermore, the specification provides, *inter alia*, at page 25, predicted antigenic regions that comprise epitope-bearing portions of the PDEF protein. One of ordinary skill in the art looking at the PDEF sequence would know which amino acid residues encoded by the polynucleotide of the claims could be substituted and still constitute a polypeptide which is capable of raising antibodies to the PDEF protein, and could routinely make and use the polypeptides to raise antibodies. Applicants need not disclose every species encompassed by a claim to satisfy the requirements of 35 U.S.C. § 112. *In re Angstadt*, 190 USPQ 214, 218 (C.C.P.A. 1976). Therefore, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Allowable Subject Matter

The indication that claims 203-206, 209, 212-228, 243-246, 249, 252-256, 259 and 280-287 are allowed is noted and appreciated by Applicants. (Paper No. 37.) The Examiner further indicated that claims 159-160, 162-163, 165-166, 168-169, 183, 186, 189, 192, 230 and 232 would be allowable if rewritten in independent form, and that claims 230, 232 and 264-279 would be allowable if submitted in a separate, timely amendment cancelling the non-allowable claims. *Id.*

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

In the Specification:

A new paragraph at page 6, after line 18, was inserted.

In the Claims:

The following claims 157, 159, 162, 165, 168, 173, 176, 180, 182, 185, 188, 191, 196, 199, 207, 210, 230, 231, 232, 236, 239, 247, 250, 257, 260, 264, 273 and 276 were substituted for pending claims 157, 159, 162, 165, 168, 173, 176, 180, 182, 185, 188, 191, 196, 199, 207, 210, 230, 231, 232, 236, 239, 247, 250, 257, 260, 264, 273 and 276:

157. (Once amended) An isolated polynucleotide comprising a first nucleic acid at least [90%] 95% identical to a reference nucleic acid selected from the group consisting of:

(a) a nucleic acid consisting of nucleotides 839 to 1048 of SEQ ID NO:1;

(b) a nucleic acid consisting of nucleotides 419 to 1420 of SEQ ID NO:1;

(c) a nucleic acid consisting of nucleotides 416 to 1420 of SEQ ID NO:1; and

(d) a nucleic acid consisting of the nucleotides encoding the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

159. (Once amended) The isolated polynucleotide of claim [158] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of nucleotides 839 to 1048 of SEQ ID NO:1.

162. (Once amended) The isolated polynucleotide of claim [161] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of nucleotides 419 to 1420 of SEQ ID NO:1.

165. (Once amended) The isolated polynucleotide of claim [164] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of nucleotides 416 to 1420 of SEQ ID NO:1.

168. (Once amended) The isolated polynucleotide of claim [167] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of the nucleotides encoding the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

173. (Once amended) The vector of claim 172, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

176. (Once amended) The host cell of claim 175, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

180. (Once amended) An isolated polynucleotide comprising a nucleic acid encoding a first amino acid sequence at least [90%] 95% identical to a reference amino acid sequence selected from the group consisting of:

(a) amino acids 142 to 211 of SEQ ID NO:2;

(b) amino acids 2 to 335 of SEQ ID NO:2;

(c) amino acids 1 to 335 of SEQ ID NO:2; and

(d) the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

182. (Once amended) The isolated polynucleotide of claim [181] 180, wherein said first amino acid sequence is at least 95% identical to amino acids 142 to 211 of SEQ ID NO:2.

185. (Once amended) The isolated polynucleotide of claim [184] 180, wherein said first amino acid sequence is at least 95% identical to amino acids 2 to 335 of SEQ ID NO:2.

188. (Once amended) The isolated polynucleotide of claim [187] 180, wherein said first amino acid sequence is at least 95% identical to amino acids 1 to 335 of SEQ ID NO:2.

191. (Once amended) The isolated polynucleotide of claim [190] 180, wherein said first amino acid sequence is at least 95% identical to the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

196. (Once amended) The vector of claim 195, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

199. (Once amended) The host cell of claim 198, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

207. (Once amended) The vector of claim 206, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

210. (Once amended) The host cell of claim 209, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

230. (Once amended) [The] An isolated polynucleotide [of claim 229,] comprising a nucleic acid encoding at least 100 contiguous amino acids of SEQ ID NO:2.

231. (Once amended) [An] The isolated polynucleotide of claim 229, comprising a nucleic acid [at least 95% identical to a nucleic acid] encoding at least 150 contiguous amino acids of SEQ ID NO:2.

232. (Once amended) The isolated polynucleotide of claim [231] 230, comprising a nucleic acid encoding at least 150 contiguous amino acids of SEQ ID NO:2.

236. (Once amended) The vector of claim 235, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

239. (Once amended) The host cell of claim 238, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

247. (Once amended) The vector of claim 246, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

250. (Once amended) The host cell of claim 249, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

257. (Once amended) The vector of claim 256, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

260. (Once amended) The host cell of claim 259, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

264. (Once amended) A polynucleotide comprising a nucleic acid fused in frame to a nucleotide sequence heterologous to SEQ ID NO:1, wherein said heterologous nucleotide sequence encodes a heterologous polypeptide, and wherein said nucleic acid is selected from the group consisting of:

(a) a nucleic acid encoding amino acids 279 to 287 of SEQ ID NO:2;

(b) a nucleic acid encoding amino acids 292 to 300 of SEQ ID NO:2;

(c) a nucleic acid encoding amino acids 317 to 325 of SEQ ID NO:2;

(d) a nucleic acid encoding amino acids 239 to 247 of SEQ ID NO:2;

(e) a nucleic acid encoding amino acids 272 to 280 of SEQ ID NO:2; and

(f) a nucleic acid encoding amino acids 248 to 331 of SEQ ID NO:2.

273. (Once amended) The vector of claim 272, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

276. (Once amended) The host cell of claim 275, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.